

Remarks

Claims 15 and 18 are pending. Claims 1-14, 16, 17 and 19-25 were previously cancelled.

Claim 15 has been amended to more clearly define the claim scope of the present invention.

Claim 18 has been amended for clarity and consistency.

Applicants respectfully contend no new matter is added by the amendments to the claims.

Applicants note that a Second Preliminary Amendment was filed and received by the U.S. Patent and Trademark Office on October 18, 2007. The Examiner, based upon statements in the October 29, 2007 Office Action, did not receive the Second Preliminary Amendment when the Office Action issued.

35 U.S.C. 112, first paragraph

Claims 15 and 18 stand rejected under 35 U.S.C. 112, first paragraph, as not providing enablement for "solvates, enantiomers and diastereomers" of the compounds of Claim 15. The Examiner has stated that the specification provides enablement for the preparation of the claimed compounds of Claim 15.

Applicants respectfully contend, this rejection is not applicable as the language of concern is no longer present in Claim 15. (See Second Preliminary Amendment). Applicants agree with the Examiner that the preparation of each compound of Claim 15 is shown and each compound is enabled consistent with 35 U.S.C. 112, first paragraph.

Rejection Under 35 U.S.C. 103(a)

All pending claims stand rejected under 35 U.S.C. 103(a) over WO/2004/026305 (published 1 April 2004, filed 17 September 2003, claiming priority to U.S. Provisional Application 60/412,158, filed 19 September 2002) in view of Patani and LaVoie, Chemical Reviews, 96, 3147-3176 (1996). The cited PCT reference is stated to be prior art only under 35 U.S.C. 102(e). This rejection may be overcome by, among other options, showing that WO 2004/026305 is disqualified under 35 U.S.C. 103(c) in a rejection under 35 U.S.C. 103(a).

Applicants respectfully traverse this rejection assert the reference is disqualified and request reconsideration in view of Exhibits 1-4 enclosed with this paper. Exhibits 1 and 2 are copies of the Assignment documents for the provisional and the International application WO 2004/026305. Both the provisional and WO 2004/026305 are assigned to Eli Lilly and Company. Also enclosed as Exhibits 3 and 4 are Assignments for the priority application European Patent Application 03380303.2, filed in the Spanish Receiving Office and the International Application under the Patent Cooperation Treaty (PCT) filed in the United States Patent and Trademark Office acting as Receiving Office, serial number PCT/US02/39766 (Publication Number WO

2005/066164 A1) for the present application.

Applicants contend that at the time the present invention was made, the inventors were under an obligation to assign their inventions to Eli Lilly and Company. The four Exhibits, and particularly Exhibits 3 and 4, evidence the inventors complied with their obligation and, in fact, assigned all rights to their invention to Eli Lilly and Company. Applicants respectfully contend the enclosed Assignment exhibits evidence the cited reference (also assigned to Eli Lilly and Company; Exhibits 1 and 2) is not available as 35 U.S.C. 102(e)/103(a) prior art against the presently claimed invention under 35 U.S.C. 103(c).

Applicants were all employees of Eli Lilly and Company at the time the present invention was made. They were under an obligation to assign any inventions made to Eli Lilly and Company. Assignment Exhibit 1 is recorded at Reel 017354, Frame 0769 (12 pages). Attached as Exhibit 2 is a copy of the Assignment of International Application PCT/US2003/026300 (WO 2004/026305) showing title is held by Eli Lilly and Company, recorded at Reel 020395, Frame 0817 (15 pages). Also attached as Exhibits 3 and 4 are copies of the Assignments of the inventions disclosed in the provisional patent application and the International patent application of the present patent application evidencing Eli Lilly and Company as the assignee of the inventions. Assignment Exhibit 3 is not recorded. Assignment Exhibit 4, an Assignment of International Application PCT/US04/39766 is recorded at Reel 017973, Frame 0981 (7 pages). Because the inventors of the present invention were, at the time the invention was made, under an obligation to assign and did assign such inventions to Eli Lilly and Company, Applicants respectfully contend they have clearly demonstrated under 35 U.S.C. 103(c), the WO 2004/026305 reference is not available as a 102(e)/103(a) reference against the present application.

Applicants respectfully disagree with the Examiner's characterization and application of the Patani and LaVoie (Chemical Reviews, 96, 3147-3176 (1996)) reference against the claims of the present application. In view of the disqualification of Blanco-Pillado, et al. (WO 2004/026305) under 35 U.S.C. 103(c), no further discussion is believed necessary to overcome the rejection based on a combination of the references.

Double Patenting Issues

Claims 15 and 18 were provisionally rejected under the non-statutory judicially created obviousness-type double patenting doctrine over Claims 18, 19, 20, 25, 26, 27 and 28 of co-pending Application No. 10/532,960 in view of Patani and LaVoie. Applicants respectfully traverse this rejection and request reconsideration.

Applicants note the October 29, 2007 Office Action refers to Application 10/532,960 (see paragraph 8, page 6) which is directed to a "Golf Training Mat" as shown by IFW entry "Claims" dated 27 April 2005. Other references by the Examiner are directed to Blanco-Pillado, et al. Further remarks assume the application number specified by the Examiner is an inadvertent error

and the Examiner intended to specify Application 10/526,960 which is the pending National Phase U.S. application corresponding to WO 2004/026305.

Initially, Applicants point out Blanco-Pillado, et al., WO 2004/026305 has been eliminated for obviousness purposes of 35 U.S.C. 102(e)/103(a) under the provisions of 35 U.S.C. 103(c). Applicants respectfully contend the pending claims in Blanco-Pillado, et al. are directed toward twenty-two compounds or pharmaceutically acceptable salts thereof; particular salts of specific compounds; and a pharmaceutical composition of a compound (22 compounds) or pharmaceutically acceptable salt thereof, in association with a carrier, diluent and/or excipient. (see IFW entries A.PE, CLM and REM dated 18 October 2007).

The presently claimed invention (following the Second Preliminary Amendment) is directed toward seventeen specific compounds or a pharmaceutically acceptable salt thereof (Claim 15) and a pharmaceutical composition comprising a compound of Claim 15 in association with a carrier, diluent and/or excipient.

Applicants contend the Examiner has not properly applied the “one-way” test for obviousness double patenting. The one-way test for obviousness double patenting essentially requires the evaluation: Do the application's claims define an obvious variation of a claim in an earlier issued patent or pending application?

Applicants contend there is no evidence in the Blanco-Pillado, et al. pending claims teaching the substitutability of the substituent groups on the pyridine ring as claimed in the present application. Further, Applicants respectfully contend the Examiner has asserted “obviousness” of Claims 15 and 18 of the present application for obviousness-type double patenting over Claims 18-20 and 25-28 of Blanco-Pillado in view of Patani and LaVoie without supporting discussion directed to compound as a whole structural similarities and differences. The Office Action dated October 29, 2007, fails to support the asserted “obviousness.”

Applicants maintain that Patani and LaVoie does not support an obviousness rejection at least because it does not disclose similar skeletal structures or uses for compounds as claimed in the present application. Patani and LaVoie state the ability of a group of bioisosteres to elicit similar biological activity has been attributed to common physiochemical properties. The physiochemical properties referred to by Patani and LaVoie include electronegativity, steric size and lipophilicity and correlating those values to the observed biological activity. A basic skeleton of a biologically active molecule must be present. The observed biological activity must be correlated with some substituents on the skeleton. This presumes the necessity of a substituent at a particular position on a molecule.

The successful interchange of an atom or group on an active skeleton for one use is not predictive of a successful interchange on a structurally different active skeleton for a different use. A potential interchange represents, at best, one of a myriad number of possible approaches to modulate biological activity of an active skeleton in a desired manner. There is no reasonable assurance of a successful modulation through use of a suggested bioisostere.

Assuming, only for purposes of discussion, Patani and LaVoie is applicable, the substitution options as applied by the Examiner (NH₂ group for OH group in carboxylates; fluorine for H atom) does not teach or suggest the various substituent groups on the pyridine ring as claimed in the present application. Necessarily, the pending claims in Blanco-Pillado, et al. in combination with Patani and LaVoie does not create a prima facie case of obviousness against the pending claims in the present application. These substituent groups in the pending claims include -C(N)-O-CH₂CH₃; -C(NOH)NH₂; -C(NH)NH₂; 4,5-dihydro-1H-imidazol-2-yl; 4,5,6,7-tetrahydro-1H-[1,3]diazepin-2-yl; 1,4,5,6-tetrahydro-pyrimidin-2-yl; -C(NCN)NH₂; 2H-tetrazol-5-yl; 1H-imidazol-2-yl; and -C(NH)NH-CH₂-CH(OCH₃)₂.

In addition, the presently claimed invention provides alternatives to the phenyl, pyridine and pyrazine rings as claimed in Blanco-Pillado, et al. These alternatives include a 6-benzo[d]isoxazol-3-ylamine and 6-1H-indazol-3-ylamine which are bicyclic fused ring groups. There is no teaching in the pending claims of Blanco-Pillado, et al. of the substitutability of these fused ring systems as claimed in the present application for the monocyclic phenyl, pyridine or pyrazine rings in Blanco-Pillado, et al. Assuming Patani and LaVoie is applicable, this reference does not fill in the deficient teaching.

It is respectfully contended, double patenting depends entirely on what is *claimed* in an issued *patent*, or co-pending application. Obviousness relates to what is disclosed (whether or not claimed) in a prior art reference (whether or not a patent). A prior art reference that renders claimed subject matter obvious under 35 U.S.C. 103 does not necessarily create an obviousness-type double patenting situation.

Applicants believe they have fully responded, and overcame, all matters raised in the October 29, 2007 Office Action and respectfully request favorable consideration of the present invention, as claimed.

Respectfully submitted,

/John C. Demeter/

John C. Demeter
Attorney for Applicants
Registration No. 30,167
Phone: 317-276-3785

Eli Lilly and Company
Patent Division
P.O. Box 6288
Indianapolis, Indiana 46206-6288

January 25, 2008

ASSIGNMENT

WHEREAS we, Maria-Jesus Blanco-Pillado; Mark Donald Chappell; Marta Garcia De La Torre; James Erwin Fritz; William Glen Holloway; James Edward Matt, Jr.; Charles Howard Mitch; Steven James Quimby; Miles Goodman Siegel; Dana Rae Smith; Russell Dean Stucky; Kumiko Takeuchi; Elizabeth Marie Thomas; and Chad Nolan Wolfe, have made an invention which is the subject of a PROVISIONAL PATENT APPLICATION, titled, OPIOID RECEPTOR ANTAGONISTS, filed September 19, 2002, as application Serial No. 6042158 (hereinafter the "Application"); and

WHEREAS ELI LILLY AND COMPANY, an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire our entire right, title, and interest in the Application and in all inventions disclosed in the Application;

NOW, THEREFORE, in consideration of good and valuable consideration, the receipt of which is hereby acknowledged, we hereby sell, assign, transfer and set over unto Eli Lilly and Company, its successors and assigns (collectively, "Lilly") our entire right, title, and interest in, the Application and in all inventions disclosed therein; all rights of priority thereto pursuant to the International Convention for the Protection of Industrial Property; any and all present or future patent applications to such inventions that may be filed in the United States or any foreign country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications under the Patent Cooperation Treaty ("PCT"), United States provisional patent applications, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates, copyrights, trademarks, and data package exclusivity rights; and any and all Letters Patent of the United States and of all foreign countries and all related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by us had this Assignment and sale to Lilly not been made.

For ourselves and for our heirs, successors and legal representatives, we covenant that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this Assignment.

For ourselves and for our heirs, successors and legal representatives, we further covenant and agree with Lilly that upon request we and they will, without further consideration than that now paid, but at the expense of Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Lilly any facts known to us or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations,

assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Lilly or its nominees, in the United States and in all other countries where Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Lilly and to vest and confirm in Lilly or its nominees the full and complete legal and equitable title to all such Letters Patent and related intellectual property.

IN WITNESS WHEREOF we have executed this assignment on the date indicated below.

9/25/2002
Date

Maria-Jesus Blanco
Maria-Jesus Blanco-Pillado

UNITED STATES OF AMERICA

STATE OF INDIANA)
COUNTY OF MARION)

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Maria-Jesus Blanco-Pillado and acknowledged the execution of the foregoing instrument this 25th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires
Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

9/24/2002
Date

Mark Donald Chappell
Mark Donald Chappell

UNITED STATES OF AMERICA

STATE OF INDIANA)
COUNTY OF MARION)

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Mark Donald Chappell and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires
Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

9/24/02

Date


Marta Garcia De La Torre

UNITED STATES OF AMERICA

STATE OF INDIANA)

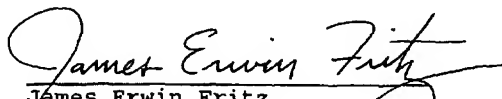
COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Marta Garcia De La Torre and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.


Notary Public

My Commission Expires

Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

9/24/2002
Date
James Erwin Fritz

UNITED STATES OF AMERICA

STATE OF INDIANA)

COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared James Erwin Fritz and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.


Notary Public

My Commission Expires

Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

9-24-02

Date

William Glen Holloway
William Glen Holloway

UNITED STATES OF AMERICA

STATE OF INDIANA)

COUNTY OF MARION)

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared William Glen Holloway and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis

Hendricks County

My Commission Expires

February 11, 2008

9/24/2002

Date

James Edward Matt, Jr.
James Edward Matt, Jr.

UNITED STATES OF AMERICA

STATE OF INDIANA)

COUNTY OF MARION)

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared James Edward Matt, Jr. and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis

Hendricks CountyMy Commission Expires

February 11, 2008

Sept. 24, 2002
Date

Charles Howard Mitch
Charles Howard Mitch

UNITED STATES OF AMERICA

STATE OF INDIANA)
COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Charles Howard Mitch and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

Sept. 24, 2002
Date

Steven James Quimby
Steven James Quimby

UNITED STATES OF AMERICA

STATE OF INDIANA)
COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Steven James Quimby and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

Sept. 24, 2002
Date

Miles Goodman Siegel
Miles Goodman Siegel

UNITED STATES OF AMERICA

STATE OF INDIANA)

COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Miles Goodman Siegel and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis
Hendricks County

My Commission Expires
February 11, 2008

9/24/2002
Date

Dana Rae Smith
Dana Rae Smith

UNITED STATES OF AMERICA

STATE OF INDIANA)

COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Dana Rae Smith and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis
Hendricks County

My Commission Expires
February 11, 2008

9-24-02
Date

Russell Dean Stucky
Russell Dean Stucky

UNITED STATES OF AMERICA

STATE OF INDIANA)
COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Russell Dean Stucky and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

9-24-02
Date

Kumiko Takeuchi
Kumiko Takeuchi

UNITED STATES OF AMERICA

STATE OF INDIANA)
COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Kumiko Takeuchi and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

9-24-02

Date

Elizabeth M. Thomas
Elizabeth Marie Thomas

UNITED STATES OF AMERICA

STATE OF INDIANA)

COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Elizabeth Marie Thomas and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

9-24-02

Date

Chad N. Wolfe
Chad Nolan Wolfe

UNITED STATES OF AMERICA

STATE OF INDIANA)

COUNTY OF MARION

Before me, a Notary Public for Hendricks County, State of Indiana, personally appeared Chad Nolan Wolfe and acknowledged the execution of the foregoing instrument this 24th day of September, 2002.

Susan L. Buis
Notary Public

My Commission Expires

Susan L. Buis
Hendricks County
My Commission Expires
February 11, 2008

ASSIGNMENT

WHEREAS we, Nuria Diaz Buezo and Concepcion Pedregal-Tercero, have made an invention which is the subject of a PROVISIONAL PATENT APPLICATION, titled, OPIOID RECEPTOR ANTAGONISTS, filed September 19, 2002, as application Serial No. ~~604/2,158~~ (hereinafter the "Application"); and

WHEREAS ELI LILLY AND COMPANY, an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire our entire right, title, and interest in the Application and in all inventions disclosed in the Application;

NOW, THEREFORE, in consideration of good and valuable consideration, the receipt of which is hereby acknowledged, we hereby sell, assign, transfer and set over unto Eli Lilly and Company, its successors and assigns (collectively, "Lilly") our entire right, title, and interest in, the Application and in all inventions disclosed therein; all rights of priority thereto pursuant to the International Convention for the Protection of Industrial Property; any and all present or future patent applications to such inventions that may be filed in the United States or any foreign country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications under the Patent Cooperation Treaty ("PCT"), United States provisional patent applications, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates, copyrights, trademarks, and data package exclusivity rights; and any and all Letters Patent of the United States and of all foreign countries and all related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by us had this Assignment and sale to Lilly not been made.

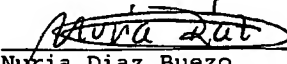
For ourselves and for our heirs, successors and legal representatives, we covenant that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this Assignment.

For ourselves and for our heirs, successors and legal representatives, we further covenant and agree with Lilly that upon request we and they will, without further consideration than that now paid, but at the expense of Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Lilly any facts known to us or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations,

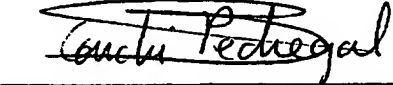
assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Lilly or its nominees, in the United States and in all other countries where Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Lilly and to vest and confirm in Lilly or its nominees the full and complete legal and equitable title to all such Letters Patent and related intellectual property.

IN WITNESS WHEREOF we have executed this assignment on the date indicated below.

9-25-2002
Date


Nuria Diaz Buezo

9-25-2002
Date


Concepcion Pedregal-Tercero

ASSIGNMENT

WHEREAS,

Dana Rae Benesh
13287 Beckwith Drive
Westfield, Indiana 46074
Citizenship: USA

Maria Jesus Blanco-Pillado
11874 Gray Eagle Drive
Fishers, Indiana 46037
Citizenship: Spain

Mark Donald Chappell
541 Pitney Drive
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James Erwin Fritz
9757 North Moonstone Place
McCordsville, Indiana 46055
Citizenship: USA

William Glen Holloway
9590 East 600 South
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Citizenship: USA

James Edward Matt, Jr.
11436 Harlequin Lane, Apt. 413
Fishers, Indiana 46038
Citizenship: USA

Charles Howard Mitch
3210 Grove Parkway
Columbus, Indiana 47203
Citizenship: USA

Concepcion Pedregal-Tercero
Lilly, S.A.
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28108 Alcobendas
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Citizenship: Spain

Steven James Quimby
10657 Kestrel Court
Noblesville, Indiana 46060
Citizenship: USA

Miles Goodman Siegel
1708 West 74th Place
Indianapolis, Indiana 46260
Citizenship: USA

Russell Dean Stucky
6045 Barth Avenue
Indianapolis, Indiana 46227
Citizenship: USA

Kumiko Takeuchi
6342 Robinsrock Drive
Indianapolis, Indiana 46268
Citizenship: USA

Elizabeth Marie Thomas
798 Robin Road
Lexington, KY 40502
Citizenship: USA

Chad Nolan Wolfe
16096 Tenor Way
Noblesville, Indiana 46060
Citizenship: USA

are inventors or co-inventors (with the persons listed above) of an invention that is the subject of a patent application ("Application") which is entitled DIARYL ETHERS AS OPIOID RECEPTOR ANTAGONIST, containing 552 pages and 0 sheets of drawings, and which:

- ☐ is being filed:
☒ was filed:

- ☐ in the United States Patent and Trademark Office
- ☐ in the United Kingdom Patent Office
- ☐ in the European Patent Office
- ☐ in the Spanish Patent Office as a European Application
- ☒ as an international application under the Patent Cooperation Treaty ("PCT"), with United States Patent and Trademark Office acting as Receiving Office

on 17 September 2003 and accorded serial number PCT/US03/26300;

and

WHEREAS ELI LILLY AND COMPANY, an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire the entire interest in all inventions disclosed in such Application;

NOW, THEREFORE, in consideration of my employment, any agreements related thereto, or other good and valuable consideration, the receipt of which is hereby acknowledged, I hereby assign to Eli Lilly and Company, its successors and assigns (collectively "Lilly") my entire right, title and interest in, to and under the Application, including all priority rights for other countries arising therefrom, all inventions therein disclosed, and any and all present or future patent applications to such inventions that may be filed in any country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications filed under the PCT, United States provisional patent applications, subsequent United States provisional patent applications claiming some or all of this invention, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates; and any related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by me had this Assignment and sale to Lilly not been made.

For myself and for my heirs, successors and legal representatives, I covenant that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this Assignment.

For myself and for my heirs, successors and legal representatives, I further covenant and agree with Lilly that upon request I and they will, without further consideration than that now paid, but at the expense of Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Lilly any facts known to me or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations, assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Lilly or its nominees, in the United States and in all other countries where Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Lilly and to vest and confirm in

Lilly or its nominees the full and complete legal and equitable title to all such Letters Patent and related intellectual property.

I have executed this assignment on the date indicated below.

1/15/2008
Date

Dana Rae Benesh
Dana Rae Benesh

1/15/2008
Date

Maria Jesus Blanco Villado
Maria Jesus Blanco Villado

1/9/08
Date

Mark Donald Chappell
Mark Donald Chappell

1/9/08
Date

James Erwin Fritz
James Erwin Fritz

Jan. 9, 2008
Date

William Glen Holloway
William Glen Holloway

1/9/2008
Date

James Edward Matt, Jr.
James Edward Matt, Jr.

1/9/2008
Date

Charles Howard Mitch
Charles Howard Mitch

1/9/2008
Date

Steven James Quimby
Steven James Quimby

Jan. 9, 2008
Date

Miles Goodman Siegel
Miles Goodman Siegel

9 Jan 2008
Date

Russell Dean Stucky
Russell Dean Stucky

Jan 9, 2008
Date

Kumiko Takeuchi
Kumiko Takeuchi

9-Jan-2008
Date

Chad Nolan Wolfe
Chad Nolan Wolfe

ASSIGNMENT

WHEREAS,

Dana Rae Benesh
13287 Beckwith Drive
Westfield, Indiana 46074
Citizenship: USA

Maria Jesus Blanco-Pillado
11874 Gray Eagle Drive
Fishers, Indiana 46037
Citizenship: Spain

Mark Donald Chappell
541 Pitney Drive
Noblesville, Indiana 46062
Citizenship: USA

Marta Garcia De La Torre
Lilly, S.A.
Avda. Industria, 30
28108 Alcobendas
Madrid, Spain
Citizenship: Spain

Nuria Diaz Buezo
Lilly, S.A.
Avda. Industria, 30
28108 Alcobendas
Madrid, Spain
Citizenship: Spain

James Erwin Fritz
9757 North Moonstone Place
McCordsville, Indiana 46055
Citizenship: USA

William Glen Holloway
9590 East 600 South
Zionsville, Indiana 46077
Citizenship: USA

James Edward Matt, Jr.
11436 Harlequin Lane, Apt. 413
Fishers, Indiana 46038
Citizenship: USA

Charles Howard Mitch
3210 Grove Parkway
Columbus, Indiana 47203
Citizenship: USA

Concepcion Pedregal-Tercero
Lilly, S.A.
Avda. Industria, 30
28108 Alcobendas
Madrid, Spain
Citizenship: Spain

Steven James Quimby
10657 Kestrel Court
Noblesville, Indiana 46060
Citizenship: USA

Miles Goodman Siegel
1708 West 74th Place
Indianapolis, Indiana 46260
Citizenship: USA

Russell Dean Stucky
6045 Barth Avenue
Indianapolis, Indiana 46227
Citizenship: USA

Kumiko Takeuchi
6342 Robinsrock Drive
Indianapolis, Indiana 46268
Citizenship: USA

Elizabeth Marie Thomas
798 Robin Road
Lexington, KY 40502
Citizenship: USA

Chad Nolan Wolfe
16096 Tenor Way
Noblesville, Indiana 46060
Citizenship: USA

are inventors or co-inventors (with the persons listed above) of an invention that is the subject of a patent application ("Application") which is entitled DIARYL ETHERS AS OPIOID RECEPTOR ANTAGONIST, containing 552 pages and 0 sheets of drawings, and which:

- ☐ is being filed:
☒ was filed:

- ☐ in the United States Patent and Trademark Office
- ☐ in the United Kingdom Patent Office
- ☐ in the European Patent Office
- ☐ in the Spanish Patent Office as a European Application
- ☒ as an international application under the Patent Cooperation Treaty ("PCT"), with United States Patent and Trademark Office acting as Receiving Office

on 17 September 2003 and accorded serial number PCT/US03/26300;

and

WHEREAS ELI LILLY AND COMPANY, an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire the entire interest in all inventions disclosed in such Application;

NOW, THEREFORE, in consideration of my employment, any agreements related thereto, or other good and valuable consideration, the receipt of which is hereby acknowledged, I hereby assign to Eli Lilly and Company, its successors and assigns (collectively "Lilly") my entire right, title and interest in, to and under the Application, including all priority rights for other countries arising therefrom, all inventions therein disclosed, and any and all present or future patent applications to such inventions that may be filed in any country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications filed under the PCT, United States provisional patent applications, subsequent United States provisional patent applications claiming some or all of this invention, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates; and any related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by me had this Assignment and sale to Lilly not been made.

For myself and for my heirs, successors and legal representatives, I covenant that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this Assignment.

For myself and for my heirs, successors and legal representatives, I further covenant and agree with Lilly that upon request I and they will, without further consideration than that now paid, but at the expense of Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Lilly any facts known to me or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations, assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Lilly or its nominees, in the United States and in all other countries where Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Lilly and to vest and confirm in

ASSIGNMENT

WHEREAS,

Dana Rae Benesh
13287 Beckwith Drive
Westfield, Indiana 46074
Citizenship: USA

Maria Jesus Blanco-Pillado
11874 Gray Eagle Drive
Fishers, Indiana 46037
Citizenship: Spain

Mark Donald Chappell
541 Pitney Drive
Noblesville, Indiana 46062
Citizenship: USA

Marta Garcia De La Torre
Lilly, S.A.
Avda. Industria, 30
28108 Alcobendas
Madrid, Spain
Citizenship: Spain

Nuria Diaz Buezo
Lilly, S.A.
Avda. Industria, 30
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on 17 September 2003 and accorded serial number PCT/US03/26300;

and

WHEREAS ELI LILLY AND COMPANY, an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire the entire interest in all inventions disclosed in such Application;

NOW, THEREFORE, in consideration of my employment, any agreements related thereto, or other good and valuable consideration, the receipt of which is hereby acknowledged, I hereby assign to Eli Lilly and Company, its successors and assigns (collectively "Lilly") my entire right, title and interest in, to and under the Application, including all priority rights for other countries arising therefrom, all inventions therein disclosed, and any and all present or future patent applications to such inventions that may be filed in any country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications filed under the PCT, United States provisional patent applications, subsequent United States provisional patent applications claiming some or all of this invention, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates; and any related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by me had this Assignment and sale to Lilly not been made.

For myself and for my heirs, successors and legal representatives, I covenant that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this Assignment.

For myself and for my heirs, successors and legal representatives, I further covenant and agree with Lilly that upon request I and they will, without further consideration than that now paid, but at the expense of Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Lilly any facts known to me or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations, assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Lilly or its nominees, in the United States and in all other countries where Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Lilly and to vest and confirm in

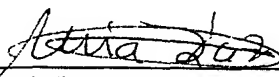
Lilly or its nominees the full and complete legal and equitable title to all such Letters Patent and related intellectual property.

I have executed this assignment on the date indicated below.

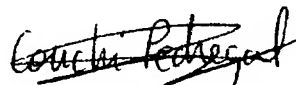
20/DEC/2007
Date


Marta Garcia De La Torre

20/Dec/2007
Date


Nuria Diaz Buezo

20/Dec/2007
Date


Concepcion Pedregal-Tercero

ASSIGNMENT

WHEREAS I, am an inventor or co-inventor (with the persons listed below) of an invention that is the subject of a patent application ("Application") which is entitled OPIOID RECEPTOR ANTAGONISTS, containing 61 pages and 0 drawings, and which:

☐ is being filed:

☒ was filed:

☐ in the United States Patent and Trademark Office

☐ in the United Kingdom Patent Office

☐ in the European Patent Office

☒ in the Spanish Receiving Office as a European application

☐ as an international application under the Patent Cooperation Treaty ("PCT"), with:

☐ United States Patent and Trademark Office acting as Receiving Office, or

☐ International Bureau acting as Receiving Office;

on December 22, 2003 and accorded application number 03380303.2;

and

WHEREAS ELI LILLY AND COMPANY, an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire the entire interest in all inventions disclosed in such Application;

NOW, THEREFORE, in consideration of my employment, any agreements related thereto, or other good and valuable consideration, the receipt of which is hereby acknowledged, I hereby assign to Eli Lilly and Company, its successors and assigns (collectively "Lilly") my entire right, title and interest in, to and under the Application, including all priority rights for other countries arising therefrom, all inventions therein disclosed, and any and all present or future patent applications to such inventions that may be filed in any country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications filed under the PCT, United States provisional patent applications, subsequent United States provisional patent applications claiming some or all of this invention, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates; and any related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by me had this Assignment and sale to Lilly not been made.


For myself and for my heirs, successors and legal representatives, I covenant that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this Assignment.

For myself and for my heirs, successors and legal representatives, I further covenant

and agree with Lilly that upon request I and they will, without further consideration than that now paid, but at the expense of Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Lilly any facts known to me or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations, assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Lilly or its nominees, in the United States and in all other countries where Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Lilly and to vest and confirm in Lilly or its nominees the full and complete legal and equitable title to all such Letters Patent and related intellectual property.

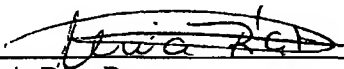
IN WITNESS WHEREOF I have executed this assignment on the date indicated below.

2/2/04
Date



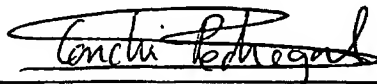
Maria Garcia De La Torre
C/Victor de la Serna
16, esc. 3, 5^aD
28016, Madrid, Spain
Citizenship: Spain

2/2/04
Date



Nuria Diaz Buezo
Paseo de la Chopera
No 88, 3^a2
28100 Alcobendas, Madrid, Spain
Citizenship: Spain

2/2/2004
Date



Concepcion Pedregal-Tercero
Colombia, 14, 2-A
28016, Madrid Spain
Citizenship: Spain

Feb 10, 2004
Date

Prabhakar Kondaji Jadhav
Prabhakar Kondaji Jadhav
7422 Fox Hollow Ridge
Zionsville, Indiana 46077
Citizenship: USA

UNITED STATES OF AMERICA

STATE OF INDIANA)
) SS:
COUNTY OF Marion)

Before me, a Notary Public for Johnson County, State of Indiana, personally appeared Prabhakar Kondaji Jadhav and acknowledged the execution of the foregoing instrument this 10 day of February, 2004.



Laura Warty
Notary Public
Commission Expires: March 20, 2008

2/13/2004
Date

Charles Howard Mitch
Charles Howard Mitch
3210 Grove Parkway
Columbus, Indiana 47203
Citizenship: USA

UNITED STATES OF AMERICA

STATE OF INDIANA)
) SS:
COUNTY OF Marion)

Before me, a Notary Public for Johnson County, State of Indiana, personally appeared Charles Howard Mitch and acknowledged the execution of the foregoing instrument this 13 day of February, 2004.



Laura Warty
Notary Public
Commission Expires: March 20, 2008

ASSIGNMENT

WHEREAS I, am an inventor or co-inventor (with the persons listed below) of an invention that is the subject of a patent application ("Application") which is entitled **OPIOID RECEPTOR ANTAGONISTS**, containing 62 pages and 0 drawings, and which:

☐ is being filed:

☒ was filed:

☐ in the United States Patent and Trademark Office

☐ in the United Kingdom Patent Office

☐ in the European Patent Office

☐ in the Spanish Patent Office as a European Application

☒ as an international application under the Patent Cooperation Treaty ("PCT"), with:

☒ United States Patent and Trademark Office acting as Receiving Office, or

☐ International Bureau acting as Receiving Office;

☐

on December 15, 2004 and accorded serial number PCT/US04/39766;

and

WHEREAS ELI LILLY AND COMPANY., an Indiana corporation having its principal place of business at Lilly Corporate Center, Indianapolis, Indiana 46285, wishes to acquire the entire interest in all inventions disclosed in such Application;

NOW, THEREFORE, in consideration of my employment, any agreements related thereto, or other good and valuable consideration, the receipt of which is hereby acknowledged, I hereby assign to Eli Lilly and Company, its successors and assigns (collectively "Lilly") my entire right, title and interest in, to and under the Application, including all priority rights for other countries arising therefrom, all inventions therein disclosed, and any and all present or future patent applications to such inventions that may be filed in any country, inclusive of, but not limited to, continuations, continuations-in-part, divisions, substitutions, reexaminations, reissues, international applications filed under the PCT, United States provisional patent applications, subsequent United States provisional patent applications claiming some or all of this invention, certificates of addition, utility models, petty patents, as well as all other intellectual property related to the Application, inclusive of, but not limited to, supplementary protection certificates; and any related patent term extensions which may be granted for Letters Patent with respect to the Application; all of the above to be held and enjoyed by Lilly for its own use and enjoyment to the full end of the term or terms for which such Letters Patent and related intellectual property rights may be granted, as fully and entirely as the same would have been held and enjoyed by me had this Assignment and sale to Lilly not been made.

For myself and for my heirs, successors and legal representatives, I covenant that no assignment, sale, agreement or encumbrance has been or will be made or entered into which would conflict with this Assignment.

For myself and for my heirs, successors and legal representatives, I further covenant and agree with Lilly that upon request I and they will, without further consideration than that now paid, but at the expense of Lilly: (i) execute original, provisional, substitute, continuation, divisional, continuation-in-part, reexamined, or reissued applications, amended specifications, or rightful declarations or oaths for such application; (ii) communicate to Lilly any facts known to me or them relating to such inventions or the history thereof; (iii) execute preliminary statements and testify in any interference proceedings, litigation discovery proceedings and depositions, oppositions, cancellation proceedings, priority contests, public use proceedings, administrative agency proceedings, litigation and other court actions and the like; (iv) execute and deliver any application papers, affidavits, declarations, assignments, or other instruments; and (v) do all other acts which, in the opinion of counsel for Lilly, may be necessary or desirable to secure the grant of Letters Patent and related intellectual property to Lilly or its nominees, in the United States and in all other countries where Lilly may desire to have such inventions, or any of them, patented, with specifications and claims in such form as shall be approved by counsel for Lilly and to vest and confirm in Lilly or its nominees the full and complete legal and equitable title to all such Letters Patent and related intellectual property.

IN WITNESS WHEREOF I have executed this assignment on the date indicated below.

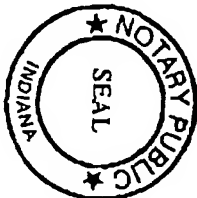
April 11, 2005
Date

Prabhakar Kondaji Jadhav
Prabhakar Kondaji Jadhav
7422 Fox Hollow Ridge
Zionsville, Indiana 46077
Citizenship: USA

UNITED STATES OF AMERICA

STATE OF INDIANA)
) SS:
COUNTY OF Marion)

Before me, a Notary Public for Marion County, State of Indiana, personally appeared Prabhakar Kondaji Jadhav and acknowledged the execution of the foregoing instrument this 11 day of April, 2005.



Rae Sneed
Notary Public
Commission Expires:

☒ Rae Sneed
Resident of Marion County
My Commission Expires:
- October 20, 2009

April 8, 2005
Date

Charles Howard Mitch
Charles Howard Mitch
3210 Grove Parkway
Columbus, Indiana 47203
Citizenship: USA

UNITED STATES OF AMERICA

STATE OF INDIANA)
COUNTY OF Marion) SS:

Before me, a Notary Public for Marion County, State of Indiana,
personally appeared Charles Howard Mitch and acknowledged the execution of the foregoing
instrument this 8th day of April, 2005.



Ree Sneed
Notary Public
Commission Expires:

Ree Sneed
President of Marion County
My Commission Expires:
October 20, 2009

Spanish Inventors:

Marta Garcia De La Torre
Lilly, S.A.
Avenida de la Industria 30
28108 Alcobendas
Madrid, Spain
Inventorship: Spain

Nuria Diaz Bueno
Lilly, S.A.
Avenida de la Industria 30
28108 Alcobendas
Madrid, Spain
Inventorship: Spain

Concepcion Pedregal-Tercero
Lilly, S.A.
Avenida de la Industria 30
28108 Alcobendas
Madrid, Spain
Inventorship: Spain

ASSIGNMENT

WHEREAS I, am an inventor or co-inventor (with the persons listed below) of an invention that is the subject of a patent application ("Application") which is entitled OPIOID RECEPTOR ANTAGONISTS, containing 62 pages and 0 drawings, and which:

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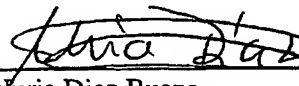
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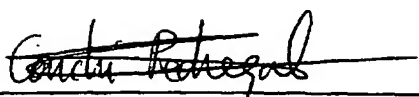
8th April 2005
Date


Marta Garcia De La Torre
Lilly, S.A.
Avenida de la Industria 30
28108 Alcobendas
Madrid, Spain
Citizenship: Spain

8 - April - 2005
Date


Nuria Diaz Buezo
Lilly, S.A.
Avenida de la Industria 30
28108 Alcobendas
Madrid, Spain
Citizenship: Spain

8-APRIL-2005
Date



Concepcion Pedregal-Tercero
Lilly, S.A.
Avenida de la Industria 30
28108 Alcobendas
Madrid, Spain
Citizenship: Spain

United States Inventors:

Prabhakar Kondaji Jadhav
7422 Fox Hollow Ridge
Zionsville, Indiana 46077
Citizenship: USA

Charles Howard Mitch
3210 Grove Parkway
Columbus, Indiana 47203
Citizenship: USA